REMARKS:

The claims have been amended to further distinguish applicant's invention from the cited prior art, as discussed below. Specifically, claim 6 is now directed to a method of reducing HIV viral load or HIV particle formation in an individual in need of such treatment. Support for this amendment may be found for example at page 24, lines 2-12 and page 28, lines 8-16 of the application as filed. Support for added claims 35-37 may be found on page 28, lines 4-6. Support for the amendment to claim 34 may be found on page 31, lines 3-8 which clearly states that the reverse transciptase and protease inhibitors are anti-HIV specific.

Regarding the USC 112 rejection regarding "protease inhibitor" and "reverse transcriptase inhibitor" in the specification and in claim 34, it is noted that claim 34 has been amended to state that the reverse transcriptase inhibitor and the protease inhibitor are HIV-specific. Thus, the claim is specifically directed to a combination of XeC and another known anti-HIV treatment, support for which may be found at at least page 31, lines 3-8 of the application as filed. Regarding the USC 112 objection to the description, it is believed that one of skill in the art, on reading the section at page 31, lines 3-8 would understand that reference is being made to anti-HIV compounds, including HIV reverse transcriptase inhibitors and HIV protease inhibitors. As the examiner will appreciate, HIV protease inhibitors and HIV reverse transcriptase inhibitors represent a small and clearly defined class of compounds.

Claims 6 and 32-33 were rejected under 35 USC 102(a) as anticipated by Mayne and the examiner has stated that "the claims are directed to preventing a malady or disease with old and well known compounds...Attempts to distance the claims from anticipated utilities with specification limitations will not be successful".

Regarding Mayne, it is believed that the amendment to the claims and the arguments below overcome this objection. Specifically, the claims have

been amended to state that administration of Xestopsongin C reduces viral load and viral particle assembly in an individual infected by human immunodeficiency virus, support for which may be found on at page 24, lines 2-12 and page 28, lines 8-16 of the application as filed.

It is noted that Mayne describes the role of tat protein in the development of HIV dementia, a neurodegenerative disorder that occurs in a subset of HIV patients. Specifically, Mayne used Xestopsongin C to determine that the tat-induced calcium release was linked to IP_3-dependent calcium release (page 6539, last paragraph on column 1 to page 6540, first paragraph, column 1) and that this increase in calcium lead to the apoptotic and/or necrotic neuronal cell death associated with HIV dementia. Based on this, Mayne "conclude[d] that pharmacological strategies that target the IP_3 pathway may be therapeutically beneficial in the treatment of HIV dementia" (page 6541, column 2, end of 2nd paragraph).

HIV dementia affects approximately 5-10% or 20% of AIDS sufferers, depending on the criteria used and the study, although it is currently believed that the actual number of cases will continue to increase as treatments increase the lifespan of AIDS patients (see for example http://www.hopkins-aids.edu/geneva/hilites_mcar_dem.html and http://www.publicaffairs.ubc.ca/media/releases/2003/mr-03-101.html). Thus, HIV dementia is a neurological disorder that develops over time and is a side-effect of AIDS that affects a portion of AIDS patients, that is, individuals infected with HIV who have developed AIDS. That is, HIV dementia is a side-effect of AIDS that develops in some individuals who have an HIV infection. The treatments for HIV dementia involve neuroprotection whereas treatments for HIV infections themselves involve reducing viral replication and/or infection, which are very different processes. Mayne suggests that it would be worth a try to see if compounds that target the IP_3 pathway could be used as neuroprotective agents for preventing neuronal cell death in patients suffering from HIV-associated dementia.

That however is not applicant's invention which is the use of XeC to reduce HIV viral load or viral particle formation. That is, Mayne does not teach or suggest using Xestospongin C as a treatment for all AIDS patients or those infected with HIV who have not yet developed AIDS as a means of reducing viral load or viral particle assembly by inhibiting NF-κB activity and thereby inhibiting viral replication. Rather, Mayne teaches that it might be "worth a try" to determine if compounds that target the IP_3 pathway C could be applied to neuronal cells as a way of preventing tat-mediated calcium release which in turn leads to neuronal cell death.

Furthermore, the prior art teachings regarding the properties of Xestospongin C in fact teaches against the use of Xestospongin C as a pharmaceutical composition. That is because given the global importance of calcium levels, physiological manipulation of calcium by blocking IP_3 receptors would be a poor choice for a treatment, as it was previously believed that NF-κB activation was calcium-dependent as discussed throughout the application as filed, for example, on page 15, lines 3-15 of the application as filed. However, it was the surprising discovery by the inventors that inhibition of NF-κB by Xestospongin C occurred independently of calcium levels that led to the discovery that Xestospongin C could be used as a pharmaceutical for treating diseases requiring NF-κB activation, as discussed throughout the application as filed, for example, on page 23, lines 3-18 and page 55, line 4 to page 57, line 22 of the specification as filed.

Thus, Mayne suggests that compounds that target the IP_3 pathway may be useful at preventing neuronal cell death in individuals having HIV dementia which developed over time as a result of having AIDS. These compounds would prevent calcium release, thereby protecting the neuronal cells. As discussed above and in the application as filed, XeC would have been seen as a poor choice for a pharmaceutical composition except possibly in instances where XeC could be applied to a localized area. HIV dementia is in effect a side-effect of an HIV infection that occurs in a subset of patients that have developed

AIDS but does not occur in all individuals who develop AIDS, as discussed above.

In summary, Mayne does not teach or suggest that XeC could be used to treat an HIV infection, wherein the infection is treated by reducing viral particle load or viral particle assembly by inhibiting NF-κB activity and thereby viral replication. Mayne at best suggests that compounds that target the IP_3 pathway may be useful at preventing neuronal cell death and as discussed above, XeC would previously have been believed to be a poor choice for a pharmaceutical composition. HIV dementia is a side-effect of AIDS that develops in some AIDS patients; it is not the same disease as an HIV infection, nor is it treated in the same way, as discussed above.

Claims 6 and 32-33 were rejected under 35 USC 103 in view of Pettit and Stingl in view of DeBarbieri. Specifically, the examiner has stated that XeD and XeE were shown by Pettit and Stingl as being useful for treating retroviral infections on the basis that DeBarbieri showed that P388 cancer cells and L1210 cancers cells have a retroviral etiology.

Regarding DeBarbieri, it is noted that this reference teaches methods for testing compounds for both anti-tumor and anti-virus activity. However, DeBarbieri, at column 5, lines 62-66 states "previous investigations of the therapeutic efficacy of drugs against these retrovirus tumor models have indicated that many agents capable of eliminating tumor cells had limited or no effect on retroviral replication". Thus, DeBarbieri states that it is in fact surprising that the compounds described therein have both anti-tumor and anti-retroviral properties and that this is clearly not the norm. Stingl and Pettit on the other hand teach the use of XeE and XeD as a treatment for breast cancer and leukemia respectively, not as treatments for retroviral infections. While it is clear that the cell lines taught by DeBarbieri could be used to test compounds for anti-retroviral activity, it is not clear that this was done by either Stingl or Pettit and that if this was in fact found to be the case, it would have been surprising and unexpected, as taught by DeBarbieri and as discussed above. Thus, Stingl and Pettit did not show that XeE or XeD could be used to treat a retroviral infection but that these

compounds could be used to treat cancer based on results from administering these compounds to cancer cell lines. Based on DeBarbieri, it would in fact have been surprising if these compounds did have anti-retroviral activity but such activity is not taught or suggested by Stingl or Pettit.

Claim 34 was rejected under USC 103 as unpatentable over Pettit and Stingl in view of DeBarbieri in further view of Rideout on the basis that Rideout teaches AZT as useful for treating HIV infections and that it would be obvious to combine two compounds for treating the same disease. It is believed that the amended claims and above arguments overcome this objection, as the prior art clearly does not teach or suggest the use of XeC to treat an HIV infection.

Further and more favorable consideration is respectfully requested.

Respectfully submitted

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CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent And Trademark Office on the date shown below.

DATE: October 22, 2004

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Michael R. Williams